

Guidelines for Managing Financial Conflicts of Interest In Human Subjects Research at NIH

The need for more substantial ethical guidance regarding conflicts of financial and other interests is pressing for NIH, where the trust and protection of research subjects is vital to our mission to improve the public health. These guidelines outline how the NIH will seek to ensure the integrity of human subjects research by preventing real or perceived conflicts of financial interest as investigators work with industry partners to promote technology transfer to meet this goal.

I. What are a clinical investigator's potential conflicts of interest?

All clinical investigators have primary obligations. These include obtaining knowledge that will promote health and health care and ensuring the safety and health of research participants. Clinical investigators may also have other, secondary interests, which could include teaching trainees, supporting a family, and earning income. These secondary interests are not, themselves, unethical, but in some circumstances, they have the potential to compromise, or appear to compromise, the judgment of clinical researchers regarding their primary obligations. When these secondary interests could compromise judgment, there is a conflict between the secondary and primary interests.

These Guidelines are meant to minimize the potential for any compromise of judgment as the result of a financial conflict, thereby ensuring both the integrity of our research and the safety of participants.

II. To Whom Do the Guidelines Apply?

The guidelines apply to all individuals who substantively participate in the development, conduct, or analysis of clinical research protocols, or in the oversight of human subjects research at the NIH. This includes everyone who can affect the integrity of research results or the safety of research participants in clinical protocols.

In particular the guidelines apply to:

- o **Principal Investigators**
- o **Associate Investigators** -- i.e., all persons whose names appear on a protocol and who are responsible for obtaining consent from patients who are to participate in a clinical trial.

Because the financial interests of an Investigator's family and outside interests may be closely allied to the Investigator's interests, with respect to financial interests (Section III, below) the term "Investigator" also includes an employee-investigator's spouse, dependent children, or household members, and any outside entity or foundation in which any of these persons have a financial interest or intellectual relationship that

could be directly affected by the conduct of the research. In multicenter studies, this applies only to investigators at the NIH Clinical Center.

- o **Affiliate Investigator:** These investigators are named on the protocol facesheet but are not responsible for obtaining consent from a patient. These individuals would not be subject to the guidelines outlined here.

III. What Interests Fall under the Guidelines for Principal Investigators and Associate Investigators?

- o Serving as an officer or in a decision-making role for a sponsor of the human subjects research;
- o Holding stock, stock options or bonds in a commercial sponsor of the human subjects research;
- o Receiving compensation for service as consultant or advisor to a commercial sponsor of the human subjects research (excluding expenses);
- o Receiving honoraria from a commercial sponsor of the human subjects research;
- o Accepting payment from the human subjects research sponsor for non-research travel or gifts;
- o Obtaining royalties or being personally named as an inventor on patents (or invention reports) for the product(s) being evaluated in the human subjects research or products that could benefit from the human subjects research;
- o Receiving payments based on research outcomes; or
- o Having other relationships with commercial sponsors of the human subjects research.

IV How the Guidelines Will Work.

The NIH has established this system to manage financial conflicts for **Principal Investigators and Associate Investigators** in clinical research. The system is designed to ensure fairness, efficiency, consistency, and flexibility.

Employees are reminded that applicable authorities prohibit them from having, for instance, outside activities, gifts from prohibited sources, or compensation from outside entities related to the performance of official duties from/with commercial sponsors of clinical research in which they participate.

A. Disclosure Reports

- The **Principal Investigators and Associate Investigators** listed on each protocol will report any interest described in Section III with commercial sponsors of the human subjects research. This information can be reported using ProtoType or an IC specific form.
- Disclosure forms will be forwarded to the Investigator's Clinical Director (CD) and Scientific Director (SD).
- If no conflict is noted, both the SD and CD sign off on the report. Reports will be sent quarterly to the DDIR. They will have NO personal identifiers.
- If any conflict is noted, the Clinical Director and Scientific Director will devise a management action.

B. Conflict Management

An investigator with conflicts real or apparent may participate in the planning, design, or other roles in a study provided the IC institutes an appropriate plan for managing the financial and decision-making conflicts. The SD and CD shall consult, if necessary, with the Deputy Ethics Counselor for the IC, with representatives of OIR and OGC Ethics Division, and the Chair of the IRB to assess the conflicts and, devise a management action.

Possible options in a management action could include any or all of the following:

- Disclosure of the conflicting decision-making and/or financial interest of the Investigator to the research subjects (usually in the consent form)
- Reassigning responsibilities from an Investigator with a conflict or the appearance of financial bias to another investigator without a financial interest in the human subjects research.
- Establishing a Data Safety Monitoring Board (DSMB) or some other independent group (such as an external audit) for overseeing protocol integrity, data analysis, and the safety of research subjects.
 - Recusal of Investigators from various roles, such as determining eligibility of research subjects, obtaining informed consent, grading and reporting adverse events, or analyzing and reporting data.
 - Where the potential conflict consists solely of an investigator's receipt of royalties that are legislatively mandated by NIH technology transfer authority,

this information should be reported to research subjects via the consent form.
(See section V below for details)

- o Waiver.

C. IRB Review of Proposed Management Action

The proposed management plan for Investigator conflicts will be sent to the Institutional Review Board for concurrence when the IRB reviews the protocol and supporting documents. Ultimately, for the study to proceed, the IRB must approve the conflict management actions for all studies, new and ongoing, and the discussion must be documented in the minutes. The IRB, when approving a protocol, will outline in its minutes to the Clinical Center what type of conflict has been identified and how this was managed. As is done presently for all protocol documents, this information will be kept in the Office of Protocol Services

D. Current Protocols

Protocols that are presently active and which include participation of Investigators with a significant conflict must update the information provided to research subjects at the time of the annual review. New research subjects enrolled will receive the updated informed consent, which reveals the conflict. Research subjects who are already on study will be apprised of the Investigator's significant interest by letter.

E. Accounting to the DDIR

After the Institute develops its management action for handling a conflict of interest, this action and reasons for any deviation from the established prohibitions and recommendations will be reported to the DDIR on a quarterly basis or more quickly if the case is time-sensitive.

V. How will NIH Intellectual Property and Royalties Be Handled?

In some instances, NIH clinical protocols will evaluate or potentially benefit product(s) in which NIH (i.e. the government) owns patents or has filed invention reports. In such cases:

- o An NIH investigator may participate at any capacity in the clinical trial, even if the investigator is listed on the patent or invention report and/or may receive royalty payments from the product(s) being tested.

- When such an investigator participates in a trial, there should be full disclosure of the relationship to the IRB and to the research subjects (i.e., information should appear in the consent form).
- In the case of ongoing protocols where this occurs, investigators should provide a new consent form or correspondence outlining the relationship.
- An independent group, such as a DSMB or external audit, must review the results of all such human subjects research.
- These relationships must be reported to the DDIR, but should not impede the pursuit of the trial.

Clinical Investigator Decision Making and Financial Interest Disclosure Form (on ProtoType or IC specific Form)

Name of Principal/Associate Investigator or Research Monitor:

Name of Research Protocol:

Sponsors of the Human Subjects Research:

Institute to which Research Protocol Submitted:

NIH regards an "Investigator" to mean the principal investigator and any other person who is responsible for the design, conduct or reporting of research funded by PHS... For purposes of the requirements of this subpart relating to financial interests, "Investigator" includes the Investigator's spouse and dependent children, household member or any outside entity or foundation in which any of the above has a financial or intellectual relationship which could be directly affected by the conduct of the research study.

All questions pertain to the last 12 months

Investigator's Disclosure	No Relationship or Interest	Relationship or Interest
Serving as an officer or in a decision making role for a sponsor of the human subjects research		
Holding stock, stock options or bonds in a commercial sponsor of the human subjects research		
Receiving compensation for service as consultant or advisor to a commercial sponsor of the human subjects research (excluding expenses)		
Receiving honoraria from a commercial sponsor of the human subjects research.		
Accepting payment from the human subjects research sponsor for non-research travel or gifts		
Obtaining royalties or being personally named as an inventor on non-NIH patents (or invention reports) for the product(s) being evaluated in the human subjects research or products that could benefit from the human subjects research (NIH patents are addressed elsewhere)		
Receiving payments based on research outcomes		
Having other relationships with commercial sponsors of the human subjects research		
Stocks or interests in competing companies with potentially conflicting products known to you		

NIH Intellectual Property

Does the Investigator have patents or invention reports (either held directly or through the NIH) that could be affected in any way by the proposed clinical study?

NO _____

YES: _____

Please list Patent or Invention Report name(s) and number(s)

If YES, _____

(Michael: Need to develop standard language to insert into consent forms for these occasions)

False statements warning inserted here

I certify that, to the best of my knowledge, all of the above information is true and accurate. I understand that any false statement may subject me to disciplinary action and a willful false certification is a criminal offense (18 U.S. C. 1001)

Signature

date

